

which exclusive *exo*-methyl migration is considered to be compelling evidence for the intervention of non-classical carbonium ions in norbornane system rearrangements. Hence the present rearrangements are assumed to involve such ions.

It should be pointed out that, subsequent to work on camphene racemization<sup>9</sup> in this laboratory, it has been shown that tricyclene intervenes to the extent that our postulate of an *endo*-methyl migration as part of the racemization process may be ruled out.<sup>14</sup> Thus the camphene anomaly cited by Berson, *et al.*,<sup>13</sup> ceases to exist, and exclusive *exo*-methyl migration in this system appears to be the rule.<sup>15</sup>

(14) P. Hirsjärvi, K. Heinonen, and L. Pirlä, *Suomen Kemistilehti*, B37, 77 (1964).

(15) We are indebted to Professor Berson for calling Hirsjärvi's work to our attention.

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## Homolytic Aromatic Substitution. VI. Phenylation of Biphenylene<sup>1,2</sup>

Sir:

Localization energies at the two sites of biphenylene have been calculated and indicate that the 2 position should possess the higher reactivity.<sup>3</sup> This prediction has been confirmed for electrophilic aromatic substitution by the isolation of only the 2 isomer from numerous synthetic reactions<sup>3,4</sup> and, more recently,

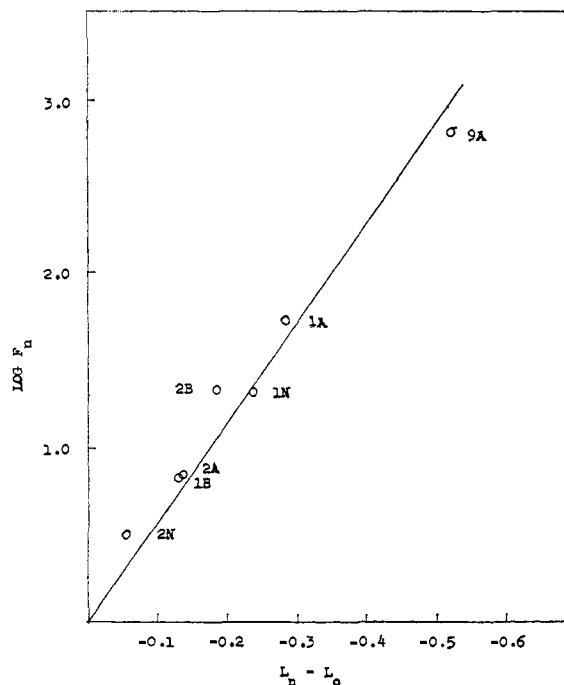


Figure 1. Correlation of partial rate factors for homolytic phenylation of anthracene (A), biphenylene (B), and naphthalene (N) with the respective differences in localization energies ( $L_n - L_0$ ).

phenylations of biphenylene are listed in Table I. The identities of those compounds in the reaction mixtures having the same retention times as authentic samples of 1- and 2-phenylbiphenylenes<sup>8</sup> were confirmed by collection from the gas chromatograph and subsequent comparison of ultraviolet spectra. Meer-

Table I. Homolytic Phenylation of Biphenylene<sup>a</sup>

Runs	Source	Orientation, %		T.r.f.	Rec., % <sup>b</sup>	Yield, % <sup>c</sup>
		1-	2-			
1-9	M <sup>d</sup>	24.3 ± 0.8	75.7 ± 0.8	19.2 ± 0.8	100 ± 3 <sup>f</sup>	2.9 ± 0.1
1-6	NAA <sup>e</sup>	22.6 ± 0.7	77.4 ± 0.7	19.4 ± 0.6	90 ± 3	6.4 ± 0.6

<sup>a</sup> Analyses by g.l.p.c. with internal standards. The uncertainties are average deviations from the mean. <sup>b</sup> Total recovery of biphenylene as unreacted biphenylene and phenylbiphenylenes. <sup>c</sup> Average yields based on biphenylene. <sup>d</sup> M, Meerwein phenylation in aqueous acetone-benzene. <sup>e</sup> NAA, N-nitrosoacetanilide in benzene. <sup>f</sup> Corrected for an 8% loss during the workup prior to analysis.

by studies of rates of tritioderprotonation and detritiation.<sup>5,6</sup> However, almost nothing is known concerning the reactivity of biphenylene in radical reactions.<sup>7</sup> We now report partial rate factors for homolytic aromatic substitution of biphenylene and an evaluation of theoretical predictions concerning the reactivity of this arene.

Percentage compositions, total rate factors, recoveries, and yields for Meerwein and N-nitrosoacetanilide

(1) Part V: S. C. Dickerman and I. Zimmerman, *J. Am. Chem. Soc.*, 86, 5048 (1964).

(2) Supported in part by an Institutional Grant (IN-146) from the American Cancer Society to New York University.

(3) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, Chapter 11.

(4) W. Baker and J. F. W. McOmie, "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Wiley-Interscience, New York, N. Y., 1959, Chapter 2.

(5) A. Streitwieser, Jr., and I. Schwager, *J. Am. Chem. Soc.*, 85, 2855 (1963).

(6) J. M. Blatchly and R. Taylor, *J. Chem. Soc.*, 4641 (1964).

(7) The reaction of biphenylene with lead tetraacetate has been reported to give 2-hydroxybiphenylene in very low yield: ref. 4, p. 89.

wein and N-nitrosoacetanilide phenylations of biphenylene, like naphthalene,<sup>9</sup> yield essentially identical total rate factors and orientation data. The mechanism of both the Meerwein<sup>10</sup> and N-nitrosoacetanilide<sup>11</sup> methods of arylation have been discussed recently.

Partial rate factors, calculated from the data for Meerwein phenylation in Table I, are 7.0 and 22 for the 1 and 2 positions, respectively. These findings are qualitatively in agreement with the corresponding localization energies but not the free valences.<sup>3</sup> For quantitative evaluation, the partial rate factors for homolytic phenylation of biphenylene, naphthalene,<sup>9</sup>

(8) W. Baker, A. J. Boulton, C. R. Harrison, and J. F. W. McOmie, *Proc. Chem. Soc.*, 414 (1964).

(9) S. C. Dickerman and G. B. Vermont, *J. Am. Chem. Soc.*, 84, 4150 (1962).

(10) S. C. Dickerman, A. M. Felix, and L. B. Levy, *J. Org. Chem.*, 29, 26 (1964).

(11) C. Ruchardt and B. Freudenberg, *Tetrahedron Letters*, 48, 3623 (1964).

and anthracene<sup>9</sup> are plotted in Figure 1 against the respective localization energies. The slope of this correlation, determined by the method of least squares, corresponds to  $\beta = -8.0 \pm 0.8$  kcal. at the 0.95 confidence level.<sup>12</sup> Since the partial rate factors for phenylation of naphthalene and anthracene are correlated by  $\beta = -7.8 \pm 0.8$  kcal.,<sup>9</sup> we conclude that biphenylene possesses "normal" reactivity in homolytic phenylation.<sup>13</sup>

Recently Streitwieser and Schwager<sup>5</sup> measured rates of tritioderprotonation of biphenylene in tritiated trifluoroacetic acid-70% perchloric acid at 25° and concluded that their findings were in serious quantitative disagreement with molecular orbital predictions. This conclusion was based upon a comparison of the found ratios of reactivities at the two sites in biphenylene ( $k_2/k_1 = 64$ ) with a predicted ratio of 4. The latter ratio appears to have been calculated from localization energies and a reaction constant based on deuterio-deprotonation in a different medium. Blatchly and Taylor<sup>6</sup> have also studied rates of detritiation of labeled biphenylenes in anhydrous trifluoroacetic acid at 70° and have found a rate ratio ( $k_2/k_1$ ) of 135. The most extensive data for this type of electrophilic aromatic substitution are those of Eaborn and Taylor,<sup>14</sup> who measured rates of detritiation of biphenyl and naphthalene at 25° in a trifluoroacetic acid-perchloric acid medium. A plot of these data and those of Streitwieser and Schwager for biphenylene against the respective localization energies exhibits such enormous scatter that one is tempted to speculate that solvation effects are position dependent and that any correlations are reaction-site dependent.

In view of the problems associated with interpreting rate data for this simple example of electrophilic aromatic substitution, it appears that homolytic aromatic substitution is the preferred reaction for evaluating predications based on molecular orbital calculations.

(12) C. A. Bennett and N. L. Franklin, "Statistical Analysis in Chemistry and the Chemical Industry," John Wiley and Sons, Inc., New York, N. Y., 1954, Chapter 6.

(13) Examination of Figure 1 reveals small deviations from linearity which could be ascribed to steric factors. Discussion of this and other considerations is deferred to full publication.

(14) C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1012 (1961).

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## A New Synthesis of Phosphatidic Acids by Direct Acylation of DL- $\alpha$ -Glycerophosphate

Sir:

Diacyl glycerophosphates are conventionally synthesized by phosphorylation of diglycerides.<sup>1-5</sup> At-

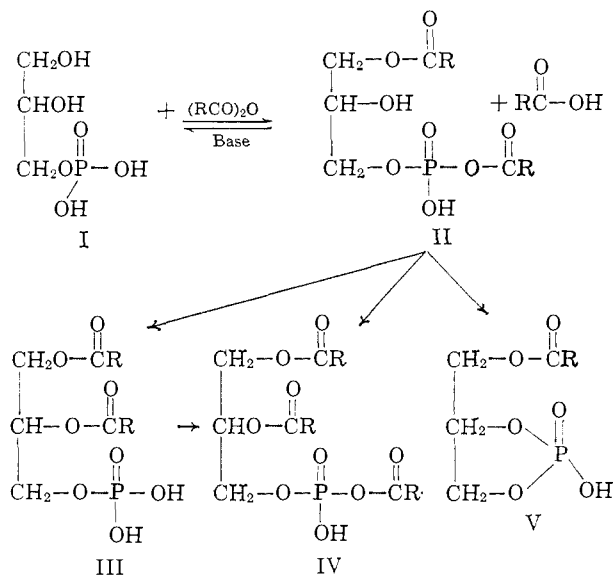
(1) E. Baer, *J. Biol. Chem.*, **189**, 235 (1951).  
(2) J. H. Uhlenbroek and P. E. Verkade, *Rec. Trav. Chim.*, **72**, 395 (1953).

(3) L. W. Hessel, I. D. Morton, A. R. Todd, and P. E. Verkade, *ibid.*, **73**, 150 (1954).

(4) E. Baer and D. Buchnea, *Arch. Biochem. Biophys.*, **78**, 294 (1958).

(5) N. Z. Stanacev and M. Kates, *Can. J. Biochem. Physiol.*, **38**, 297 (1960).

tempts at direct acylation of glycerophosphate failed to give pure diacylglycerophosphate<sup>6,7</sup> since now we know that large amounts of cyclic phosphate (V) are formed in such a reaction. It is known that the reaction of an acylation agent with phosphomonoesters rapidly gives an acyl phosphate.<sup>8</sup> In the case of  $\alpha$ -glycerophosphate (I) the corresponding acyl phosphate (II) could give 1',2'-cyclic phosphate (V)<sup>9</sup> or alternatively it could cause acylation of the neighboring 2' hydroxyl group to give III (the latter would then again rapidly form the mixed anhydride IV). The acylation of the primary hydroxyl group will occur in the normal fashion. Acylation of the 2'-hydroxyl group would probably also occur by direct attack of the acid anhydride on II. Intramolecular cyclic phosphate diester formation is a property of a variety of phosphate esters which bear a hydroxyl group adjacent to the phosphate such as ribonucleoside 2'- (or 3'-) phosphates and sugar phosphates.<sup>10</sup> Lapidot and Khorana<sup>11-13</sup> found that acetylation and benz-



oylation of ribonucleoside 3'-phosphates with the corresponding anhydrides in the presence of tetraethylammonium salt produce 2',5'-diacyl ribonucleoside 3'-phosphate as a sole product, and no cyclic phosphate could be detected. A similar approach has been applied in the present work for the development of a simple method for the preparation of phosphatidic acids by direct acylation of DL- $\alpha$ -glycerophosphate with fatty acid anhydrides in the presence of the appropriate tetraethylammonium salt. Thus, dicaproyl, dipalmitoyl, and dioleoyl DL- $\alpha$ -glycerophosphate were prepared in good yields (70-80%).

In a typical experiment, a mixture of pyridinium DL- $\alpha$ -glycerophosphate (0.4 mmole) and tetraethylammonium palmitate (4 mmoles) was rendered anhydrous by repeated addition of dry pyridine and subse-

(6) I. Kabashima, *Ber.*, **71**, 1073 (1938).

(7) H. Arnold, *ibid.*, **74**, 1736 (1941).

(8) A. W. D. Avison, *J. Chem. Soc.*, 732 (1955).

(9) T. Ukita, N. A. Bates, and H. E. Carter, *J. Biol. Chem.*, **216**, 867 (1955).

(10) H. G. Khorana, "Some Recent Developments in the Chemistry of Phosphate Esters of Biological Interest," John Wiley and Sons, Inc., New York, N. Y., 1961.

(11) Y. Lapidot and H. G. Khorana, *Chem. Ind. (London)*, 166 (1963).

(12) D. H. Rammler, Y. Lapidot, and H. G. Khorana, *J. Am. Chem. Soc.*, **85**, 1989 (1963).

(13) Y. Lapidot and H. G. Khorana, *ibid.*, **85**, 3857 (1963).